

REMARKS

Status of the claims:

Because the Examiner did not enter the amendment of the claims as was filed with the response of July 8, 2004, Applicant herein submits a response without amending the claims. Accordingly, claims 2-13, 17-19, and 22-40 are pending and ready for further action on the merits. Reconsideration is respectfully requested in light of the following remarks.

Rejections under 35 USC §103

Claims 2-9, 11, 13, 17-19, 22-35, and 38-40 are rejected under 35 USC §103(a) as allegedly being unpatentable over Hersh '791 (US Patent No. 5,667,791).

Claims 2, 6, 7, 9-12, 17-19, 28-31, and 34-40 are rejected under 35 USC §103(a) as allegedly being unpatentable over Hillebrand '500 (US Patent No. 5,296,500).

Present Invention

The present invention, as recited in claim 2, relates to a preparation for topical application comprising the following components:

- (a) at least one salt selected from alkali metal salts, alkaline earth metal salts and other minerals,
- (b) at least one amino acid in pure form,
- (c) zinc oxide and/or an inorganic peroxide, and
- (d) at least one secondary plant substance selected from the group consisting of carotinoids, phytosterols, saponins, polyphenols, flavonoids, terpenes, phytoestrogens, sulfides, phytin acid, dietary fibers and combinations thereof.

As recited in claim 3, the instant invention further comprises e) at least one polyunsaturated fatty acid of vegetable sources in addition to the components that are in claim 2.

Applicant has found that the combination of zinc oxide and/or inorganic peroxides improves the microcirculation in the cell. This improvement can be both visually and biometrically shown. The improvement is further increased by the use of at least one salt and at least one secondary plant substance.

Disclosure of Hersh '791

Hersh '791 discloses a composition of glutathione and selenomethionine in a topical carrier and method of using the composition to reduce and repair x-ray radiation-induced skin damage.

Hersh '791 fails to disclose a composition containing as least one amino acid in pure form.

Disclosure of Hillebrand '500

Hillebrand '500 discloses a method for regulating wrinkles and/or atrophy in mammalian skin comprising treating the skin with a safe and effective amount of the amino acid derivative N-acetyl-L-cysteine and/or a derivative thereof.

Hillebrand '500 fails to disclose at least one amino acid in pure form.

Removal of the Rejection over Hersh '791

Applicant respectfully points out that neither Hersh '791 nor Hillebrand '500 disclose at least one amino acid in pure form.

Applicant submits that amino acids are carboxylic acids having one or more amino groups ($-NH_2$) in the molecule. In the technical field of the present invention amino acids are divided into essential, semi-essential and non-essential amino acids. The about 20 different α -amino acids found in proteins are rather simple organic compounds having the general structure $R-CH(NH_2)-COOH$, in which an amino group and a side-chain (R) are attached alpha to the carboxyl functionality. The R group may be aliphatic, aromatic, or heterocyclic (Applicant directs the

Examiner's attention to reference 2, page 57, paragraph bridging left and right column that was filed with the response of July 8, 2004).

It should be noted that important commonly known amino acids are encoded. The coding of cystine is CysCys (please see reference 3, middle of page 65 that was submitted with the response of July 8, 2004). The person of ordinary skill in the art of the present invention would not regard selenomethionine used in Hersh '791 as a commonly known amino acid in free form. In the literature considered as belonging to the general knowledge of a person skilled in the art selenomethionine is described as "selenium-containing amino acid". It has been further described as a compound, which is (only) comparable with the essential amino acid methionine. In comparison to the amino acid methionine, in selenomethionine, the sulfur atom has been replaced by a selenium atom. That is, this compound contains a metal element and is therefore regarded as an organometallic compound. An organometallic compound is different from an organic amino acid wherein the substituent R may be aliphatic, aromatic or heterocyclic. Furthermore, it should be emphasized that selenomethionine is a commonly used selenium source for orally administering selenium to mammals. Feeding studies showed that organically bound selenium, such as selenomethionine, is incorporated several times faster into the

body tissue than inorganic selenium (see enclosed Ullmann's Encyclopedia of Industrial Chemistry, volume A28, page 465, left column, 4th paragraph). This is also confirmed by Hersh '791 in column 4, lines 13 to 19 and column 8, lines 20 to 25. It should be emphasized that Hersh '791 describes selenomethionine as "selenium-containing seleno amino acid" and not as amino acid in free form (please note column 8, lines 21 and 22). The person of ordinary skill in the art would interpret the term "amino acid" as it is usually used in the technical field. The inventor of the present invention, who is an expert in the technical field of the present invention, is absolutely sure that every person skilled in the technical field of the present invention would interpret the term "amino acid" to mean an "amino acid in free form" that is usually known in the technical field. The term "amino acid" does not include "amino acid derivatives" or "proteins" or "proteids". This is evidenced by the references that were submitted with the response of July 8, 2004 and with the attached references. Again, the term "amino acid" only comprises well-defined compounds of organic carboxylic acids in free form having unsubstituted amino groups. The selenomethionine used in Hersh '791, therefore, is not included within said term. It should be emphasized again that it is well-known to the person of ordinary skill in the art that selenomethionine is a usual selenium source. This is also

confirmed by Hersh '791. In this compound, as mentioned above, the sulfur atom of the essential amino acid methionine has been replaced by the metal atom selenium. Since the essential part of the use of selenomethionine is the provision of selenium, which is also confirmed by Hersh '791, the use of this compound cannot provide any teaching or suggestion with respect to any amino acids in free form. In view of this essential fact the disclosure content of Hersh '791 cannot teach or suggest a composition of the present invention. Thus, the rejection is inapposite. Withdrawal of the rejection over Hersh '791 is warranted and respectfully requested.

Removal of the Rejection over Hillebrand '500

Hillebrand '500 also fails to describe an amino acid in free form. Hillebrand '500 describes a method for regulating wrinkles or atrophy in mammalian skin using a composition comprising N-acetyl-L-cysteine or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier. The teaching of Hillebrand '500 is to use N-acetyl-L-cysteine or a pharmaceutically acceptable salt thereof for regulating wrinkles (see column 1, penultimate paragraph). In the section entitled "Zinc Salts" from column 3, last paragraph to column 5, 1st paragraph, Hillebrand '500 indicates that the compositions are rendered substantially odorless by adding a zinc salt. The zinc

most likely removes odors by complexing with malodorous H_2S , which may be formed in trace amounts as the active compound decomposes (see column 3, lines 56 to 62). Similar to Hersh '791, Hillebrand '500 does not describe any composition comprising an amino acid in pure form. N-acetyl-L-cysteine is an amino acid derivative. Furthermore, Hillebrand '500 does not teach a combination of an amino acid in pure form and zinc oxide and/or inorganic peroxide. In column 7, penultimate paragraph of Hillebrand '500, there is a list of compounds disclosed, with "soybean saponins" being one in this list with a multiplicity of other compounds. Nothing in Hillebrand '500 points particularly to the group of secondary plant substances. Moreover, nothing in Hillebrand '500 points to any improving effects of a composition comprising an amino acid in pure form, zinc oxide and/or inorganic peroxide acid SPS. Further, there is no hint in Hillebrand '500 that by the specific combination of components of the present invention health improving substances, particularly SPS's, can be infiltrated better into the cell. Applicant submits there is no motivation for a person of ordinary skill in the art to replace the amino acid derivative in an example of Hillebrand '500 by any amino acid in pure form and, in addition thereto, add SPS in a pharmaceutically effective amount. It is absolutely incorrect, as alleged by the Examiner, that the skilled artisan would have a reasonable

expectation of success by doing this since Hillebrand '500 is absolutely silent concerning any effects of a combination of amino acid, zinc oxide and SPS. Therefore, Hillebrand '500 cannot render obvious the instant invention because Hillebrand '500 fails to disclose the elements of the instant invention. Withdrawal of the rejection over Hillebrand '500 is warranted and respectfully requested.

With the above remarks, it is believed that the claims, as they now stand, define patentable subject matter such that passage of the instant invention to allowance is warranted. A Notice to that effect is earnestly solicited.


If any questions remain regarding the above matters, please contact Applicant's representative, T. Benjamin Schroeder (Reg. No. 50,990), in the Washington metropolitan area at the phone number listed below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: 6) Remington's Pharmaceutical Sciences, Fifteenth Edition, Ed. Hoover, 1975, page 513

7) Printout of Webmed.ch/docs/selen visited July 29, 2004

8) Ullmann's Encyclopedia of Industrial Chemistry, volume A28, page 465

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Liothyronine I 125 or I 131

Triiodothyronine I 125 (or I 131); ¹²⁵I-labeled T-3 (or I 131);
Liothyronine I 181 (Nuclear Consultants); Tressitope (Squibb);
Triomet (Abbott)

Liothyronine labeled with either ¹²⁵I or ¹³¹I by mild oxidation. For the structure of liothyronine, see page 909.

Preparation—By the exchange of crystalline synthetic hormone with ¹³¹I under carefully controlled conditions. Since such reactions always result in a mixture of products, purification must be effected by column and/or paper strip chromatography.

Uses—For *in vitro* evaluation of thyroid function. ¹²⁵I-labeled T-3, added to an aliquot of the patient's serum, along with a source of secondary binding sites (Sephadex, ion-exchange resin, etc.), will become bound to binding sites on thyroxine-binding proteins (TBP) not occupied by thyroxine. ¹²⁵I-labeled T-3 not bound to TBP becomes bound to the secondary binding sites in which form it is separated from the serum and measured, thereby providing an estimate of unoccupied binding sites on the TBP.

Note—Due to the high specific activity required, radiation damage can easily take place. This is in part prevented by the use of propylene glycol (50%) as a solvent. Packages should be refrigerated or even frozen during storage, and should not be used longer than 2 weeks.

Note—In making dosage calculations, correct for radioactive decay; for radiological constants, see Table II.

Dose—Not for internal use.

**Oleic Acid I 125 and I 131
Triolein I 125 and I 131**

Oleotape I-125 (Squibb); Oleic Acid I 125 (Nuclear Consultants);
Raoleic Acid-131 (Abbott); Oleotape and Oleotape Diagnostic (Squibb);
Oleic Acid I 131 (Nuclear Consultants);
Triolein I 125 (Nuclear Consultants);
Raoleic-131 (Abbott); Triolein I 131 (Nuclear Consultants);
Trioleotape (Squibb)

Oleic acid or triolein, which has been iodinated by mild oxidation of ¹²⁵I or ¹³¹I to form iodostearic acid ¹²⁵I (or ¹³¹I) or triiodostearin ¹²⁵I (or ¹³¹I), respectively.

Preparation—Iodinated triolein is prepared by the action of iodine monochloride on the highly purified fat triolein, in a carbon tetrachloride solution. After removal of the solvent, and also all "free iodine," it is diluted with peanut oil to an activity of about 1 mCi/ml. The iodine bond is relatively stable in the digestive tract, but it is liberated as the molecule is metabolized in the blood stream and tissues.

Iodinated oleic acid is prepared in a similar manner and has similar properties.

Uses—As diagnostic agents for measuring fat absorption in suspected pancreatic disease or other gastrointestinal dysfunction. The use of these agents is based on the fact that the triolein, requiring pancreatic lipase for hydrolysis prior to passage through the gastrointestinal wall, is not absorbed in cases of pancreatitis and cystic fibrosis, while the free acid, not requiring such hydrolysis, is taken up in the normal fashion. The assay for extent of absorption may be made on blood samples taken 2 to 8 hours after administration, or on 24- to 36-hour stool samples.

Note—In making dosage calculations, correct for radioactive decay; for radiological constants, see Table II.

Dose—Oral (capsules or oral solution), 25 to 50 μ Ci.

Selenomethionine Se 75

Selenomethionine-75 (Diagnostic Isotopes); L-Selenomethionine-Se 75 (Amersham Searle)

An isotonic, sterile pyrogen-free solution of L-selenomethionine containing an ⁷⁵Se radioactive tag [7246-06-2]. Selenomethionine is the selenium analog of the naturally occurring amino acid methionine. The general biochemistry of selenomethionine and methionine are therefore very similar. See *Methionine* (page 964).

Preparation—Extracted from yeast grown on a sulfur-free medium to which trace amounts of sodium selenite, labeled with ⁷⁵Se, have been added. After hydrolysis of the yeast, protein as ⁷⁵Se-labeled amino acid is separated.

Uses—For scintigraphy of the pancreas and parathyroid glands. It has also been used to visualize the parotid and prostate glands.

Note—In making dosage calculations, correct for radioactive decay; for radiological constants, see Table II.

Dose—100 to 250 μ Ci.

Sodium Chloride Na 22

Sodium Chloride Na 22 (Abbott; Nuclear Consultants)

A sterile, pyrogen-free solution of sodium chloride ²²Na [171.12-21-9] suitable for injection.

Preparation—Cyclotron-produced by bombarding ²⁴Mg with deuterons. The reaction is ²⁴Mg(d, α)²²Na.

Uses—As an injection for the determination of circulation times, sodium space, and total exchangeable sodium. While the use of ²²Na has certain advantages over the use of ²⁴Na in medicine, its half-life of only 15 hours creates problems of supply and the usual tracer dose of ²²Na is well within the accepted tolerance level. Because ²²Na emits positrons it can be detected readily by coincidence counting methods which combine the advantages of low background activity with high resolution.

Note—In making dosage calculations, correct for radioactive decay; for radiological constants, see Table II.

Dose—Intravenous, 5 to 10 μ Ci.

Sodium Chromate Cr 51 Injection USP

Chromic acid (H₂CrO₄), disodium salt; Chromitope Sodium (Squibb);
Rachromate-51 (Abbott)

Disodium chromate (Na₂CrO₄) [7775-11-3]. **Injection USP:** A sterile solution of radioactive ⁵¹Cr processed in the form of sodium chromate in water for injection. For those uses where an isotonic solution is required, sodium chloride may be added in appropriate amounts as provided under *Injections*, page 1461. The specific activity is not less than 10 mCi/mg of sodium chromate at the end of the expiration period. Other forms of radioactivity do not exceed 10% of the total radioactivity.

Preparation—By neutron bombardment of enriched ⁵⁰Cr.

Description—**Injection USP:** Clear, slightly yellow solution; pH between 7.5 and 8.5.

Uses—A biological tracer to measure circulating red-cell volume, red-cell survival time, and whole-blood volume (red-cell mass and plasma volume). To tag erythrocytes, a sample of the patient's blood or of donor blood is mixed with a solution of Na₂⁵¹CrO₄ and allowed to remain until the isotope diffuses into cells (15 to 60 min). Once inside the cell, the bivalent chromate anion (CrO₄⁻²) is reduced to the trivalent chromic cation (Cr³⁺), which firmly associates with the globin portion of the cell contents. The unbound chromium (in the plasma) is either reduced with ascorbic acid or removed by washing the cells. The treated blood or suspension of cells is then injected into the circulation, time allowed for complete *in vivo* mixing, and samples taken for scintillation counting. Red-cell or whole-blood volume is estimated by the radioisotope dilution method. Normal mean values for whole-blood volume obtained by the isotope method are 65.6 \pm 5.95 ml/kg.

Such tagged cells also provide an excellent means of studying red cell disappearance, as in hemolytic anemias and gastrointestinal bleeding. Platelets may also be labeled, though less effectively. For such purposes, it is essential that the specific activity be high—at least 5 to 15 mCi/mg. Such a solution, prepared by the peroxide oxidation of Cr-Cl₃, is essentially colorless.

For greatest tagging efficiency, sterile vials are available containing a special formalin ACD solution. The blood and chromate are added directly to these vials wherein tagging takes place.

Neue Entdeckungen erweitern unsere Kenntnis über die Wichtigkeit von Selen

Teil IV

Formen von Selen-Supplementen:

Die wirksamsten und sichersten Formen, unsere Ernährung mit Selen zu ergänzen, ist nicht die anorganische Salzform, sondern sind die organischen Formen Selenomethionin oder Selen-Hefe.

Selenomethionin:

Selenomethionine is a purified, selenium containing amino acid.

Selenomethionin ist eine gereinigte, Selen enthaltende Aminosäure. Es gibt keine Hefe in Selenomethionin. Es ist eine natürlich auftretende Komponente in bestimmten Lebensmitteln. Selenomethionin ist dem essentiellen Aminosäure-Methionin ähnlich, aber mit einem Selen-Atom statt einem Schwefel-Atom ausgestattet. *(Selenomethionine is comparable with the essential amino acid methionine, however has a selenium atom in place of the sulfur atom.)*

Die Form von Selenomethionin, die der Körper verwenden kann, ist L-Selenomethionin (enthalten in SELEN, gebunden an Spirulina platensis). Dieses wird besser absorbiert und besser in die Körperkomponenten integriert als jede andere bekannte Form des Selen. Forscher, die anorganisches Selen mit DL-Selenomethionin verglichen, fanden, daß DL-Selenomethionin nicht so effektiv wie das anorganische Selen war (45). DL-Selenomethionin wird zu anorganischem Selen abgebaut und an den anorganischen Selen-Körperpool zurückgegeben. Dadurch beträgt die Bioverfügbarkeit nur 1/5 des L-Selenomethionin (31).

Prof. Richard A. Passwater hat dreißig Jahre lang verschiedene Formen des Selen bei seinen Tierstudien verwendet und herausgefunden, daß die Selen enthaltenden Aminosäuren (Selenomethionin und Selenocystein) und die methylierten Selenide gegenüber den anorganischen Formen von Selen (Selenit und Selenat) in bezug auf allgemeine Gesundheit, Langlebigkeit und Krebsverhinderung vorzuziehen sind.

Selenium containing amino acid (selenomethionine and selenocysteine)

In neuseeländischen Studien wurde herausgefunden, daß Selenomethionin mindestens zu 75 Prozent biologisch verfügbar ist, verglichen mit maximal 59 Prozent biologischer Verfügbarkeit bei der Einnahme von Natriumselenit. Die Blut-Selen-Spiegel stiegen mit Selenomethionin schneller und blieben konstanter als nach der Einnahme von Natriumselenit (30-32).

In einer finnischen Studie wurde nachgewiesen, daß Selenomethionin die Blut-Selen-Spiegel auch wesentlich stärker ansteigen ließ und diese Substanz länger im Blut verblieb als anorganisches Selen (33).

In einer 1984 durchgeführten MIT-Studie wurde festgestellt, daß organische Formen des Selen (Anm.: z.B. Selen/Spirulina) in der Lage sind, den Selen-

Ullmann's Encyclopedia of Industrial Chemistry

Fifth, Completely Revised Edition

Volume A28:

Water to Zirconium and Zirconium Compounds

Editors: Barbara Elvers, Stephen Hawkins



(PER) because animal feeding tests were carried out at an assumed protein value higher than the true value. Much of the literature uses a PER value of 1.8 (cf. casein PER of 2.5).

Total yeast proteins are generally higher in lysine and deficient in sulfur amino acids, methionine, cysteine, and cystine as compared to cell-wall protein amino acid composition (see p. 462). The amino acid composition of yeasts resembles that of oil-seed proteins, particularly soy protein.

Vitamins. Most yeast species are unable to synthesize one or more vitamins and are dependent on external sources.

Yeast contains predominantly the vitamins of the B complex, and is thus an excellent source of B vitamins for human and animal nutrition.

Inactive dry yeast is frequently used as a vitamin supplement rather than as a source of protein in food formulations. Some dry yeast products are even fortified with vitamins such as B₁, B₂, and niacin to meet certain special requirements of vitamin tablet manufacturers. Although the daily requirements for most of the B vitamins are not fully met by the recommended yeast intake, their contribution to meeting the B complex vitamin requirements in the human diet is substantial. However, yeast does not provide vitamin C and fat-soluble vitamins such as A, E, K, and D. Nevertheless, dry yeast can function as a valuable vitamin source when used in combination with other food ingredients, as is generally the case with human diets.

Baker's yeast contains 7–10% ergosterol, mainly in the membranes. It serves as the precursor for vitamin D₂. This conversion occurs when ergosterol is irradiated with ultraviolet light. However, this process is not economical since synthetic vitamin D₂ is less expensive. Baker's yeast does not contain 7-dehydrocholesterol, the precursor of vitamin D₃.

Minerals. Yeasts take up substantial quantities of macro- and micronutrients from the surrounding growth medium. The mineral-ash content amounts to ca. 8% on a dry solid basis. Although the concentrations of potassium and phosphorus in dry yeast are higher than those of other elements such as Ca, Mg, and S, the mineral contributions made by an allowable daily serving of 20 g of dry yeast is minor considering the high mineral content in the bulk of an average human diet.

However, recent nutritional studies have shown that certain diets are deficient in some important trace elements. Supplementation of these diets with dry yeast has partially or wholly alleviated such dietary problems. Such inadequacies in the diet were later determined to be due to deficiencies of trace elements such as chromium, selenium, and molybdenum. Brewer's and baker's yeasts contain these elements in trace levels. Specially produced yeast products are now commercially available with higher levels of these micronutrients.

Chromium. In 1955 researchers reported that rats fed with certain nutritionally deficient diets showed impaired tolerance to blood glucose. The conditions were then reversed by supplementing the feed with brewer's yeast. It was later suggested that the active component responsible for reversing the glucose intolerance was an organic complex rich in chromium.

Diabetes, which is caused by glucose intolerance, can manifest itself in two ways. In juvenile diabetics, the pancreas fails to secrete insulin into the bloodstream. Those who are affected by another type of glucose intolerance begin to show symptoms in midlife. These patients secrete insulin into the bloodstream but cannot control their blood sugar level. It is possible to correct this problem by supplementing the diet with brewer's yeast. Findings have indicated the importance of another component besides insulin for the proper control of the blood sugar level. This active component, which is a trivalent chromium complex, is now referred to as glucose tolerance factor (GTF). Patients in the second category have GTF early in life, but tend to lose it with age, causing increased vulnerability to diabetes. It is suggested that GTF functions as a cofactor for insulin, thereby enhancing the binding of insulin to receptive sites on the membranes of insulin-sensitive tissues.

Other investigations showed a reduction in the level of cholesterol and triglycerides in the blood of humans supplementing their diets with brewer's yeast rich in GTF. However, further feeding studies are necessary to confirm the results before yeast rich in GTF could be recommended as a possible treatment for lowering blood sugar or curing lipid disorders.

Selenium has been recognized as an essential trace element for both human and animal nutrition. Recent surveys in some parts of Finland show that people with blood selenium less than 0.04 µg/L are three times more prone to heart

attacks than their counterparts with normal selenium levels. Also, in China a fatal heart disease in children known as Kaishan's disease is presently treated by fortifying the diet with sodium selenite.

The importance of selenium in animal nutrition is also well documented. A common disease in lambs, white muscle disease, is due to selenium deficiency. It can be cured by adding 0.05 ppm Se to the diet.

A diet containing Se at the levels approaching toxicity is effective in lowering the incidence of some types of cancer in animals. Research findings strongly suggest that certain types of cancer can be prevented by maintaining a proper level of Se in the diet.

Early feeding studies conducted with selenite or selenate salts as sources of Se showed that the uptake of Se was quite poor. In contrast, organically bound Se, such as selenomethionine found in some natural foods, is incorporated several times faster into the body tissue than inorganic Se.

Organically bound Se is now recognized as nutritionally important because of its ability to prevent some vitamin E deficiency disorders, at least in laboratory animals fed diets partially reduced in nucleic acids.

Reports, particularly from Finland, indicate that Se deficiencies can be corrected by supplementation with Se-rich yeasts.

There are several factors that restrict Se uptake by yeast under conventional batch propagation conditions primarily because of toxic effects of Se salts on yeast growth. However, a new procedure for the propagation of food-grade Se-rich yeast has been developed, based on the concept that, under conditions of sulfur deficiency, sulfur could be replaced by selenium in yeast. The growth medium is fed incrementally so that the Se concentration never reaches toxic levels. Under these conditions the yeast assimilates Se as a reaction to sulfur deficiency. Nutritional yeasts with an intracellular Se concentration of 1000 ppm are commercially available in the United States as dietary supplements.

Lipids. The lipid content of yeasts can vary between 4 and 7% (dry basis). About 1% can be extracted directly by solvents. The determination of total lipids requires acid hydrolysis prior to solvent extraction. Major constituents are fatty acid glycerides with a predominance of palmitic and oleic acids, sterols, and lipolipids.

Carbohydrates. Total carbohydrates account for about 30–35% of the yeast cell (dry basis). They consist mainly of carbohydrate storage compounds such as glycogen, the disaccharide trehalose, and the structural materials of the cell wall: the glucans and mannans. Level of fiber in whole baker's yeast cells is about 18% (dry weight basis).

3.2. Use of Yeast as a Major Protein Source

Candida utilis yeast was used as an important human diet supplement in Germany during World War II. Sulfite waste liquor, a byproduct of the paper pulp industry, and wood hydrolysates were used as raw materials. The large-scale production of yeasts on hydrocarbon substrates was found to be infeasible for economic and safety reasons.

For use as a major source of protein by humans the presence of nucleic acid is a serious obstacle; nucleic acid nitrogen accounts for about 10–15% of the total nitrogen of yeast cells. The intake of nucleic acid leads to elevated blood plasma levels of uric acid and may cause gout. Sources of nucleic acids in the diet are meat, particularly organ meat such as liver. Beer and possibly other fermented beverages also contain nucleic acids.

Search for methods is underway to reduce the level of nucleic acids or to remove them completely, since present methods are not economical. There is no need, however, for the removal of nucleic acids from yeast biomass for use in feed.

Yeast biomass in its inactive dried form is used widely as feed supplement. It is used in poultry rations and pig starter feeds. The use of brewer's and distiller's byproduct yeast in feed has been demonstrated. In countries that lack cheap sources of oil-seed meals (mainly soy bean meal), *Candida utilis* biomass is used extensively as a protein supplement. Live yeast cells in the form of active dried yeast or yeast culture are also used in the feed industry.

Yeast culture is produced by combining slurries of baker's yeast with cereal feed grains. The mash is incubated to permit yeast multiplication and fermentation. It is then dried at temperatures that preserve yeast viability.

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